REMARKS

THE AMENDMENTS

Applicants have amended claims 1 and 2 by inserting the term "pegylated alpha-interferon" after the term "alpha-interferon or" to further clarify the scope of the interferon derivative intended.

Applicants have amended claims 3 and 4 by inserting the term "or pegylated alpha-interferon" after "alpha-interferon" to further clarify the scope of the interferon derivative intended.

Applicants have amended claims 1 and 2 to insert the phrase -- selected from the group consisting of VX-148 and VX-944 -- after the term "IMPDH inhibitor" to clarify the scope of the IMPDH inhibitors intended.

Applicants have amended claim 2 to delete the term "contains" and insert the term "comprises" after the term "composition" to maintain consistency of the type of composition intended throughout the claims.

Applicants have amended claim 4 by deleting the phrase -- wherein said optimal composition comprises alpha-interferon or a derivative thereof and an optimal amount of an IMPDH inhibitor -- after "human," by deleting the term "first amount" and replacing it with the term "standard dose" after the phrase "first composition comprising a", by deleting the term "first amount" and replacing it with the term "standard dose" after the term "concentration produced by said", by deleting the phrase "produce said optimal composition wherein" and replacing it with the phrase "a second amount of said IMPDH inhibitor such that" before the term "said ratio", and by deleting the phrase;

-- f. administering said optimal composition to said human. --

and replacing it with the phrase;

-- f. combining said second amount of said IMPDH inhibitor with said alpha-interferon or pegylated alpha-interferon to produce said optimal composition.--

Each of the above amendments to claim 4 further clarifies the steps intended for this method of producing a composition claim.

Applicants have amended method claim 8 to delete the phrase -- selected from mycophenolic acid, ribavirin, VX-497, or VX-944 -- to clarify the intended IMPDH inhibitor to VX-148 only.

Applicants have amended method claim 9 to delete the phrase -- selected from ribavirin, mycophenolic acid, or VX-497 -- and insert the term "VX-944" to clarify the intended IMPDH inhibitor.

None of the above amendments add any new matter. These amendments are further discussed below in the context of the Examiners rejections.

THE REJECTIONS

I. 35 U.S.C. § 102(b)

Claims 1-2 and 5-10 stand rejected under 35 U.S.C. § 102(b) as being anticipated by P. Glue in *Seminars in Liver Disease*, Vol. **19,** supp. 1, pp.17-24 (1999) (hereinafter "Glue") for the reasons of record in the July 15, 2002 Office Action.

Additionally, the Examiner asserts that Glue teaches co-administration of ribavirin and interferon alpha

at page 23, figure 7 "which shows co-administration of ribavirin and interferon alpha (solid bars)".

As indicated above, applicants have amended claims 1 and 2 to clarify that the IMPDH inhibitor in the optimal composition is VX-148 or VX-944. Glue discloses the IMPDH inhibitor ribavirin used in combination with interferon alpha or a pegylated interferon. Applicant's claims, as amended, do not include ribavirin within the claimed composition. Therefore, applicants believe that the composition of claim 1 and the method of claim 2 are novel over Glue. Because claims 5-7 depend either directly or indirectly from claims 1 and 2, they, too, are novel over Glue. As noted above, applicants have canceled claims 8-12. Consequently, applicants request that the Examiner withdraw this 35 U.S.C. § 102(b) rejection of claims 1, 2, and 5-10.

II. 35 U.S.C. § 103(a)

Claims 1, 2, 5-9, and 12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over M. Brunet et al. in *Transplantation Int.*, Vol. **13** suppl. 1, pp. S301-S305 (2000) (hereinafter "Brunet") in view of W. Markland et al., in *Antimicrobial Agents and Chemotherapy*, Vol. **44** (4), pp. 859-866 (2000) (hereinafter "Markland") for the reasons of record in the July 15, 2002 Office Action.

The Examiner asserts that: "[T]hat Applicant has evolved a different rationale for using a known composition at a known dose does not alter the composition, the dose, or the method of use". Specifically, the Examiner asserts that Markland teaches the use of an IMPDH inhibitor, such as mycophenolic acid (MPA), in combination with interferon alpha for treating Hepatitis C. The Examiner also asserts that Brunet teaches the 0.5-1.0 gram b.i.d. dose for MPA

claimed by applicants. The Examiner further asserts that "it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of Markland with those of Brunet to administer 0.5-1.0 grams of mycophenolic acid twice a day in combination with interferon alpha to treat hepatitis C." Applicants traverse.

As noted above, applicants have amended composition claim 1 and methods claims 2 and 5-7 to clarify that the only IMPDH inhibitor in the claimed composition or method is VX-148 or VX-944. Neither VX-148 nor VX-944 is disclosed by Brunet or Markland. Markland, by itself, or in combination with Brunet, does not teach co-administration of VX-944 or VX-148 with alpha-interferon or pegylated alpha-interferon. Thus, the presence of VX-944 or VX-148 in the claimed optimal composition, coupled with the fact that VX-944 or VX-148 is present in an amount such that the ratio of Cavg/Cmin is between 1-10, renders the claimed optimal composition unobvious over Markland, by itself, or in combination with Brunet.

Therefore, applicants believe that claims 1-2 and 5-7 are patentable over both Brunet and Markland. As noted above, applicants have canceled claims 8, 9, and 12. Consequently, applicants request that the Examiner withdraw this 35 U.S.C. § 103(a) rejection of claims 1-2 and 5-7.

Claims 1, 2, 5-9, and 11 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over T. Wright et al. in *Hepatology*, Vol. **3**,(4), p. 408A (1999) (hereinafter "Wright") in view of Markland. Specifically, the Examiner asserts that Markland teaches an IMPDH inhibitor can be used in combination with interferon alpha to treat hepatitis C and further that Wright teaches treatment of hepatitis C with VX-497 and teaches levels exemplified on page 17 of

applicant's specification. The Examiner concludes that "it would be obvious to one of ordinary skill in the art to combine the teachings of Wright with those of Markland to administer VX-497 in combination with interferon alpha to treat hepatitis C virus." Applicant's traverse.

As noted above, applicants have amended composition claim 1 and methods claims 2 and 5-7 to clarify that the only IMPDH inhibitor in the claimed composition or method is VX-148 or VX-944. Neither VX-148 nor VX-944 is disclosed by Wright or Markland. Markland, by itself, or in combination with Wright, does not teach co-administration of VX-944 or VX-148 with alpha-interferon or pegylated alpha-interferon. Thus, the presence of VX-944 or VX-148 in the claimed optimal composition, coupled with the fact that VX-944 or VX-148 is present in an amount such that the ratio of Cavg/Cmin is between 1-10, renders the claimed optimal composition unobvious over Markland, by itself, or in combination with Wright.

Therefore, applicants believe that claims 1-2 and 5-7 are patentable over both Wright and Markland. As noted above, applicants have canceled claims 8, 9, and 11. Consequently, applicants request that the Examiner withdraw this 35 U.S.C. § 103(a) rejection of claims 1-2 and 5-7.

III. 35 U.S.C. § 112, Second Paragraph

Claims 1-2 and 4-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner asserts that the recitation of "alpha interferon or a derivative" is indefinite because the term "derivative" renders it unclear as to what molecules are intended.

As noted above, applicants have amended claims 1-2 to insert the phrase "pegylated alpha-interferon" and amended claims 3-4 to insert the phrase "or pegylated alpha-interferon" to clarify the interferon derivative intended. Thus, applicants have obviated the Examiner's rejection of claims 1-4. Because claims 5-7 depend either directly or indirectly from claims 2-4, they, too, are in condition for allowance. Additionally, as noted above, applicants have canceled claims 8-12. Support for this amendment may be found at page 19, lines 3-4. Consequently, applicants request that the Examiner withdraw this 35 U.S.C. § 112 second paragraph rejection of claims 1-2 and 5-7.

Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner asserts that "while the claim is drawn to a method of producing a composition, the method steps describe a method of determining an optimal dosage." As noted above, applicants have obviated the Examiners rejection by deleting the phrase -- wherein said optimal composition comprises alpha interferon or a derivative thereof and an optimal amount of an IMPDH inhibitor -- to clarify that the method intended is that of producing an optimal composition. Additionally, applicants have added step f. to claim 4 to clarify the steps required for the intended method. Support for this amendment may be found in the specification at page 9 line 23 to page 10, line 8.

For the reasons set forth above, applicants request that the Examiner withdraw his 35 U.S.C. § 112, second paragraph rejections.

CONCLUSION

Applicants request that the Examiner enter the above amendments, consider the accompanying remarks, and allow the pending claims to pass to issue.

Respectfully submitted,

Michael C. Badia
Reg. No. 51,424
Agent for Applicants
Nandakumar Govindaswamy
Ltd. Recognition
Attorney for Applicants

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139-4242
Tel.: (617)444-6467
Fax.: (617)444-6483